

**REMARKS**

Claims 68-70, 72, 73, 75-85, and 88 are pending.

***Rejection of Claim 72 under 35 U.S.C. § 112, first paragraph***

Claim 72 was rejected under 35 U.S.C. § 112, first paragraph, because the Examiner found “no support in the instant specification for said compound.” Applicant respectfully disagrees. Support for creatine monohydrate can be found, for example, in the specification, as originally filed, at page 30, line 10. This disclosure, alone or in combination with the other teachings of the specification, would have been sufficient evidence to convey to an ordinarily skilled artisan that Applicant was in possession of the claimed invention at the time the application was filed. Therefore, Applicant respectfully requests that this rejection of claim 72 under 35 U.S.C. § 112, first paragraph be withdrawn.

***Rejection of Claims 68-70, 75-80, and 84-85 under 35 U.S.C. § 103(a)***

Claims 68-70, 75-80, and 84-85 are rejected under 35 U.S.C. § 103(a) as being obvious over Yu *et al.* (U.S. Patent No. 5,702,688) in view of Kaddurah-Daouk *et al.* (U.S. Patent No. 5,324,731 and WO 96/14063). Applicant respectfully disagrees.

Claim 68 and its dependent claims are directed to a method for increasing energy reserves in the skin of a subject who is suffering from a skin disorder associated with free-radicals, aging, sun radiation, stress or fatigue. The method includes administering to the subject an effective amount of creatine or a salt thereof. Claim 69 is directed to a method for sustaining energy production in the skin of a subject who is suffering from a skin disorder associated with free-radicals, aging, sun radiation, stress or fatigue. The method includes administering to the subject an effective amount of creatine. Claim 70 is directed to a method for modulating energy flow in the skin of a subject who is suffering from a skin disorder associated with free-radicals, aging, sun radiation, stress or fatigue. The method includes administering to a subject an effective amount of creatine or a salt thereof, such that the energy flow in the skin of said subject is modulated.

According to the Examiner, Yu *et al.*, the primary reference, describes “a treatment of abnormal skin conditions (skin aging, wrinkles, psoriasis, etc.) using an amphoteric composition comprising an effective amount of creatine or creatinine as an amphoteric compound...Applicant’s claims differ in that the claims require increasing energy reserve, sustaining energy production, and modulating energy flow in the skin.”

*Yu et al.* is directed to methods of treating skin disorders using pH balanced compositions of alphaketo acids and alphahydroxy acids. It is directed to methods and compositions using a wide variety of organic and inorganic amphoteric compounds, including creatine, to enhance the skin penetration of the “active” ingredients, i.e., alphaketoacids and alphahydroxy acids.

*Yu et al.* fails to teach or suggest that amphoteric compounds, such as creatine, would be useful in any other capacity other than to balance the pH and enhance the ability of the alphaketo acids and the alphahydroxy acids to penetrate the skin. *Yu et al.* fails to teach or suggest the claimed methods using an effective amount of creatine. *Yu et al* emphasizes that the active compounds are the alphahydroxy acids and the alphaketo acids, not the amphoteric compounds.

Applicant submits that *Yu et al.*, the primary reference, fails to teach or suggest administering an effective amount of creatine or a salt thereof to the skin of a subject who is suffering from a skin disorder associated with free-radicals, aging, sun radiation, stress or fatigue. Furthermore, *Yu et al.* also fails to teach or suggest methods for increasing energy reserves in the skin of a subject, sustaining energy production in the skin of a subject, or modulating energy flow in the skin of a subject.

Applicant submits that U.S. Patent No. 5,324,731 and WO 96/14063, the secondary references, fail to overcome the deficiencies of *Yu et al.*

According to the Examiner, U.S. Patent No. 5,324,731 describes “creatine (or its salts) and it[ ]s use in the treatment of metastasis of epithelial cells via modifying energy level...[it] teaches energy balance using creatine kinase in the treatment of other diseases such as psoriasis, wound healing, neurological disorders, and cerebrovascular diseases.”

Applicant submits that U.S. Patent No. 5,324,731 is directed to inhibiting transformation of cells in which purine metabolic enzyme activity is elevated. U.S. Patent No. 5,324,731 fails to overcome the deficiencies of *Yu et al.* Like *Yu et al.*, it does not teach or suggest administering an effective amount of creatine to the skin of a subject who is suffering from a skin disorder associated with free-radicals, aging, sun radiation, stress or fatigue. Furthermore, it also fails to teach or suggest methods for increasing energy reserves in the skin of a subject, sustaining energy production in the skin of a subject, or modulating energy flow in the skin of a subject.

WO 96/14063 also fails to overcome the deficiencies of *Yu et al.*, alone or in combination with U.S. Patent No. 5,324,731. According to the Examiner, WO 96/14063 “teaches that creatine is used for modifying energy of cells in stress via increasing energy reserve, sustaining energy production and modulating energy flow.” Like *Yu et al.*, it does not teach or suggest administering an effective amount of creatine to the skin of a

subject who is suffering from a skin disorder associated with free-radicals, aging, sun radiation, stress or fatigue.

Further, the Examiner argues that “when these references are combined together, the underlying mechanism is clearly present in the treatment of skin aging and wrinkle[s] by administering a creatine compound, taught by the Yu *et al.* reference.” Applicants disagree. As stated above, Yu *et al.* does not teach or suggest administering an effective amount of creatine to the skin of a subject who is suffering from a skin disorder associated with free-radicals, aging, sun radiation, stress or fatigue, as claimed by Applicant. Yu *et al.* is limited to treatment methods including effective amounts of alpha-hydroxy acids, not methods using effective amounts of creatine compounds as claimed by Applicant.

Therefore, Applicant respectfully requests that this rejection of claims 68-70, 75-80, and 84-85 under 35 U.S.C. § 103(a) be withdrawn.

***Rejection of Claims 68-70, and 75-88 under 35 U.S.C. § 103(a)***

Claims 68-70, and 75-88 are rejected under 35 U.S.C. § 103(a) as being obvious over Le Fur *et al.* (U.S. Patent No. 5,256,649) in view of Carniglia (U.S. Patent No. 4,871,718) Kaddurah-Daouk *et al.* (U.S. Patent No. 5,324,731 and WO 96/14063). Applicant respectfully disagrees.

The claims have been summarized above.

Le Fur *et al.* is directed to a cosmetic composition for combating aging of the skin, by administering an ademetionine (SAMe) generating system. Le Fur’s composition requires betaine, ATP or an ATP generating system, a magnesium salt, and a potassium salt. In the patent, Le Fur *et al.* teach that the combination of the betaine and the ATP generating system are important to generate ademetionine in situ to treat the skin.

Le Fur *et al.* does not teach or suggest that the ATP generating agent alone would be effective to treat the skin alone, but rather the ATP generating system is described as an ingredient with betaine which can be used to generate ademetionine which combats aging of the skin. Furthermore, Le Fur *et al.* does not teach or suggest any methods using an ATP generating system alone, let alone methods of administering creatine to the skin of a subject who is suffering from a skin disorder associated with free-radicals, aging, sun radiation, stress or fatigue, as claimed by Applicant. Le Fur *et al.’s* methods are limited to methods of treating the skin using ademetionine or precursors thereof.

The secondary references fail to overcome the deficiencies of Le Fur *et al.* According to the Examiner, Carniglia (U.S. Patent No. 4, 871,718) describes that ATP may be generated by creatine phosphate. The Examiner also relies on Kaddurah-Daouk *et al.* (U.S. Patent No. 5,324,731 and WO 96/14063) for describing that “creatine and its analogues modulate[] the energy level in skin cells via ATP utilization.” These references, alone or in combination with the primary reference, do not teach or suggest Applicants’ claimed methods, e.g., methods which include administering an effective amount of creatine to the skin of a subject who is suffering from a skin disorder associated with free-radicals, aging, sun radiation, stress or fatigue.

Therefore, Applicant respectfully requests that this rejection of claims 68-70, and 75-88 under 35 U.S.C. § 103(a) be withdrawn.

***Rejection of Claims 68-70, 72, 73, 75-85, and 88 under Judicially Created Doctrine of Obviousness-Type Double Patenting***

Claims 68-70, 72, 73, 75-85, and 88 were rejected under the judicially created doctrine of obviousness type double patenting over claims of U.S. Patent No. 6,242,491. The Office Action indicates that a timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.312 (c) may be used to overcome a rejection based on a non-statutory double patenting ground provided the patent is shown to be commonly owned with this application. It is respectfully submitted that a terminal disclaimer will be filed upon an indication of allowable subject matter, if appropriate.

**SUMMARY**

Cancellation of and/or amendments to the claims should in no way be construed as an acquiescence to any of the Examiner's objections and/or rejections. The cancellation of the claims and/or amendments to the claims are being made solely to expedite prosecution of the above-identified application. Applicants reserve the option to further prosecute the same or similar claims in the present or another patent application. The amendments made to the claims are not related to any issues of patentability.

In view of the above remarks and amendments, it is believed that this application is in condition for allowance. If a telephone conversation with Applicant's Attorney would expedite prosecution of the above-identified application, the Examiner is urged to call Elizabeth A. Hanley, Esq. at (617) 227-7400.

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